CENTER FOR DRUG EVALUATION AND RESEARCH

Application Number 64-081

CORRESPONDENCE

biocraft
LABORATORIES, INC.

Corporate Headquarters
18-01 River Road
P.O. Box 948
Fair Lawn, NJ 07410
Phone: 201-703-0400
Fax: 201-797-9491
Fax: 201-797-0015

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Fax: 201-977-8150

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Phone: 201-445-3141
Fax: 201-445-8564

5000 Christopher Drive
Mexico, MO 65265
Phone: 314-581-8080
Fax: 314-581-8085

July 16, 1996

FEDERAL EXPRESS
Food and Drug Administration
Office of Generic Drugs
Center for Drug Evaluation and Research
Metro Park North # 2
HFD-600
Document Control Room # 150
7500 Standish Place
Rockville, MD 20855

MINOR AMENDMENT

Our Reference:
AADA 64-081
Cefaclor Capsules USP, 250 mg 500 mg

Dear Staff:

This letter is in response to the deficiency letter dated June 25, 1996 concerning referenced AADA.

On July 3, 1996, Biocraft submitted written responses to the New Jersey District concerning the FDA-483 issued on June 5, 1996 following the PAI for Cefaclor Capsules, USP. In a letter dated July 12, 1996 from the New Jersey District (copy attached), Biocraft was advised that , based on our submission, the District has changed their recommendation to approvable.

In the written response, Biocraft committed to tightening the capsule weight variation specification and adding a particle size specification for the drug substance. These have been completed and will be submitted post approval as Changes Being Effected Supplement.

Sincerely,

BIOCRAFT LABORATORIES, INC.

Harmon Aronson

Harmon Aronson
Vice President of
Quality Management

HA/mb
ENC.
CC: New Jersey District

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Mid-Atlantic Region

Food and Drug Administration
Waterview Corporate Center
10 Waterview Blvd., 3rd Floor
Parsippany, NJ 07054

Telephone (201) 331-2909

July 12, 1996

Harmon Aronson, PhD
Vice President, Quality Management
Biocraft Laboratories, Inc.
18-01 River Road
Fair Lawn, New Jersey 07410

Dear Mr. Aronson:

We are in receipt of your written response dated July 3, 1996, regarding the pre-approval inspection conducted May 9 - June 5, 1996, in support of ANDA 64-081 Cefaclor Capsules, 250 & 500 mg.

Our evaluation finds your written response to FDA483 observations 1,2,3,5 and 7, adequately address the concerns raised during the inspection. Based on your submission, we have changed our recommendation for ANDA 64-081, to approvable. However, we offer the following comments with respect to the remaining observations, which we felt were not completely addressed in your response:

Blackston Hill, Chemist, Philadelphia Laboratory, ext.

Any further questions can be addressed to my attention at (201) 331-2909.

Sincerely,

Mercedes B. Mota

MERCEDES B. MOTA
Compliance Officer
New Jersey District

Biocraft Laboratories, Inc.

AADA# 64-081
Cefaclor Capsules USP,
250 mg and 500 mg

RESPONSE TO FDA DEFICIENCY LETTER

In accord with the final rule published in the Federal Register of September 8, 1993, Biocraft Laboratories, Inc. hereby certifies that the field copy is a true copy of the technical section of this submission and has been provided to the New Jersey District Office.

Harvey Richards
Associate Director
Regulatory Affairs

July 16, 1996
Date

Center

biocraft
LABORATORIES, INC.

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July 16, 1996

FEDERAL EXPRESS
Food and Drug Administration
Office of Generic Drugs
Center for Drug Evaluation and Research
Metro Park North # 2
HFD-600
Document Control Room # 150
7500 Standish Place
Rockville, MD 20855

ORIG AMENDMENT

Our Reference:
AADA 64-081
Cefaclor Capsules USP, 250 mg 500 mg

Dear Staff:

This letter is in response to the deficiency letter dated June 25, 1996 concerning referenced AADA.

On July 3, 1996, Biocraft submitted written responses to the New Jersey District concerning the FDA-483 issued on June 5, 1996 following the PAI for Cefaclor Capsules, USP. In a letter dated July 12, 1996 from the New Jersey District (copy attached), Biocraft was advised that , based on our submission, the District has changed their recommendation to approvable.

In the written response, Biocraft committed to tightening the capsule weight variation specification and adding a particle size specification for the drug substance. These have been completed and will be submitted post approval as Changes Being Effected Supplement.

Sincerely,

BIOCRAFT LABORATORIES, INC.

Harmon Aronson

Harmon Aronson
Vice President of
Quality Management

HA/mb
ENC.
CC: New Jersey District

AADA 64-081

Biocraft Laboratories, Inc.
Attention: Nora M. Buenviaje
18-01 River Road
Fair Lawn, NJ 07410

JUN 25 1996

Dear Madam:

This is in reference to your abbreviated antibiotic application dated February 19, 1993, submitted pursuant to Section 507 of the Federal Food, Drug, and Cosmetic Act, for Cefaclor Capsules USP, 250 mg (base) and 500 mg (base).

Reference is also made to your amendment dated March 31, 1995.

This application is deficient and, therefore, not approvable under 21 CFR 314.125(b)(13) because the Center for Drug Evaluation and Research (CDER) is unable to find that the methods used in, and the facilities and controls used for, the manufacture, processing, packaging or holding of the drug product comply with current good manufacturing practice (CGMP) regulations.

Our conclusion is based upon the findings revealed during an inspection of your facility located at 8-10 Gloria Lane, Fairfield, NJ 07004 by representatives of our New Jersey District Office. The inspection occurred over multiple days in May 1996 and concluded on June 5, 1996. These findings were detailed in the FD-483 issued on June 5, 1996, to Herman J. Aronson, Vice President, Quality Management.

Until such time that you can demonstrate to the Agency that the CGMP-related issues associated with the manufacture of Cefaclor Capsules USP, 250 mg and 500 mg have been corrected and the Agency's concerns are otherwise satisfied, your application cannot be approved.

You should amend this application when the CGMP-related issues have been satisfactorily resolved. Your amendment submitted in response to this not approvable letter will be considered as a MINOR AMENDMENT provided that the amendment contains no significant additional information necessary to remedy the CGMP deficiencies or to address concerns identified by the

investigators. Your amendment should include a statement from a responsible company official informing us that this application has been recommended for approval by representatives of the New Jersey District. If, as a result of follow-up inspections related to the ongoing evaluation of this or other applications, it is necessary for you to significantly revise your procedures, controls or practices to correct your deficiencies, then the amendment will be considered to represent a MAJOR AMENDMENT.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

Sincerely yours,

/S/

Frank O. Holcombe, Jr., Ph.D.
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

1964
THIRTY
YEARS
QUALITY
INTEGRITY
SERVICE
1994

biocraft®
LABORATORIES, INC.

FEDERAL EXPRESS

March 31, 1995

Office of Generic Drugs, CDER, FDA
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

FDA ORIG AMENDMENT

CORPORATE HEADQUARTERS
18-01 River Road
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Fax: 201-797-0015

AADA 64-081
CEFACLOR CAPSULES, USP, 250 mg and 500 mg

RE: MINOR AMENDMENT IN RESPONSE TO FDA DEFICIENCY LETTER HOLCOMBE TO SNYDER, DATED MARCH 14, 1995

Dear Staff:

Reference is made to the attached FDA Deficiency Letter, Holcombe to Snyder, dated March 14, 1995 regarding our AADA 64-081 on Cefaclor Capsules, USP, 250 mg and 500 mg.

In this Amendment, we have responded to each of the Comments in the said deficiency letter.

Additionally, a Field copy of this Amendment will be sent to FDA Newark District Office at Water View Corporate Center, 10 Waterview Boulevard, Parsippany, NJ 07054.

Please amend our Application accordingly.

Thank you.

Sincerely,
BIOCRAFT LABORATORIES, INC.

Nora M. Buenviaje
Regulatory Associate

RECEIVED
MAR 31 1995
GENERIC DRUGS

002

Enclosures: Review & Archival copies of Amendment

92 Route 46, P.O. Box 185
Elmwood Park, NJ 07407
Phone: 201-796-3436
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Fax: 314-581-8085

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

AADA 64-081

MAR 14 1995

Biocraft Laboratories, Inc.
Attention: Jay Snyder
18-01 River Road
Fair Lawn, NJ 07410

Dear Sir:

This is in reference to your abbreviated antibiotic application dated February 19, 1993, submitted pursuant to Section 507 of the Federal Food, Drug, and Cosmetic Act, for Cefaclor Capsules USP, 250 mg and 500 mg.

Reference is also made to your amendment dated September 20, 1994.

The application is deficient and, therefore, not approvable under Section 507 of the Act for the following reasons:

Chemistry Deficiency

It is not indicated whether or not you have established a "cut-off" point at which you discontinue the use of recycled materials and begin a new campaign. In addition please specify the maximum holding time, and holding conditions for your recycled material. Also clarify whether capsule contents will be recovered, and, if so, provide a detailed description of the process, master batch records, and specify the conditions for eligibility of a batch for recovery.

In addition to responding to this deficiency, please note and acknowledge the following in your response:

Please provide any additional stability data which are available to date.

The referenced bulk antibiotic application has not yet been approved. Until it is approved, this application will remain not approvable.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all the deficiencies listed. A partial reply will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this letter will be considered a MINOR amendment and should be so designated in your cover letter. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

Sincerely yours,

/S/

Frank O. Holcombe, Jr., Ph.D.
Acting Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

AADA 64-081

MAR 14 1995

Biocraft Laboratories, Inc.
Attention: Jay Snyder
18-01 River Road
Fair Lawn, NJ 07410

Dear Sir:

This is in reference to your abbreviated antibiotic application dated February 19, 1993, submitted pursuant to Section 507 of the Federal Food, Drug, and Cosmetic Act, for Cefaclor Capsules USP, 250 mg and 500 mg.

Reference is also made to your amendment dated September 20, 1994.

The application is deficient and, therefore, not approvable under Section 507 of the Act for the following reasons:

Chemistry Deficiency

It is not indicated whether or not you have established a "cut-off" point at which you discontinue the use of recycled materials and begin a new campaign. - In addition please specify the maximum holding time, and holding conditions for your recycled material. Also clarify whether capsule contents will be recovered, and, if so, provide a detailed description of the process, master batch records, and specify the conditions for eligibility of a batch for recovery.

In addition to responding to this deficiency, please note and acknowledge the following in your response:

Please provide any additional stability data which are available to date.

The referenced bulk antibiotic application has not yet been approved. Until it is approved, this application will remain not approvable.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all the deficiencies listed. A partial reply will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this letter will be considered a MINOR amendment and should be so designated in your cover letter. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

Sincerely yours,

/S/ 3/13/95

Frank O. Holcombe, Jr., Ph.D.
Acting Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

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September 20, 1994

Office of Generic Drugs, CDER, FDA
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Noted
Review in
turn by
Chemist
(Labeling OK)
SEP 27 1994
M Anderson
10/3/94

AADA 64-081
CEFACLOR CAPSULES, USP, 250 mg and 500 mg

RE: MAJOR AMENDMENT IN RESPONSE TO FDA DEFICIENCY LETTER, GUYER TO SNYDER, DATED AUGUST 31, 1994

AC
NDA ORIG AMENDMENT

Dear Staff:

Reference is made to FDA Deficiency letter, Guyer to Snyder, dated August 31, 1994, regarding our AADA 64-081 on Cefaclor Capsules, USP, 250 mg and 500 mg.

In this Amendment, we have answered each of the Comments listed in the FDA Deficiency Letter mentioned above.

Included in our Responses, where appropriate, are the following:

a.

b.
c.
d.

e.
f.

In addition, Biocraft hereby certifies that a Field Copy of this Amendment is being sent to the Newark District Office at 61 Main Street, West Orange, NJ 07052 under separate cover.

Please amend our Application accordingly. Thank you.

Sincerely,

BIOCRAFT LABORATORIES, INC.

Nora M. Buenviaje
Regulatory Associate

002

Attachment: Review and Archival copies of Amendment

CORPORATE HEADQUARTERS
18-01 River Road
P.O. Box 948
Fair Lawn, NJ 07410
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Fax: 201-703-9491
Fax: 201-797-0015

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5000 Christopher Drive
Mexico, MO 65265
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ORIGINAL

BIOAVAILABILITY

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Noted.
To be reviewed by BIO
Mark Anderson
10/3/94

September 8, 1994

Office of Generic Drugs, CDER, FDA
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

CORPORATE HEADQUARTERS
18-01 River Road
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AADA 64-081
CEFACLOR CAPSULES, USP, 250 mg and 500 mg

RE: BIOEQUIVALENCE AMENDMENT IN RESPONSE TO FDA DEFICIENCY LETTER, PATNAIK TO BUENVIAJE, DATED AUGUST 18, 1994

Dear Staff:

Reference is made to FDA Deficiency letter, Patnaik to Buenviaje, dated August 18, 1994, regarding our AADA 64-081 on Cefaclor Capsules, USP, 250 mg and 500 mg.

In this Amendment, we have responded to each of the Comments in the said Deficiency Letter.

Please amend our Application accordingly. Thank you.

Sincerely,

BIOCRAFT LABORATORIES, INC.

Maurice Bordoni
Director of New Products

Attachments: Review & Archival copies

002

92 Route 46, P.O. Box 185
Elmwood Park, NJ 07407
Phone: 201-796-3436
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209 McLean Blvd.
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Fax: 314-581-8085

AADA 64-081

Biocraft Laboratories, Inc.
Attention: Jay Snyder
18-01 River Road
Fair Lawn, NJ 07410

AUG 31 1994

Dear Sir:

This is in reference to your abbreviated antibiotic application dated February 19, 1993, submitted pursuant to Section 507 of the Food, Drug, and Cosmetic Act, for Cefaclor Capsules USP, 250 mg and 500 mg.

Reference is also made to your amendment dated May 12, 1994.

The application is deficient and, therefore, not approvable under Section 507 of the Act for the following reasons:

Chemistry Deficiencies

In addition to responding to these deficiencies, please note and acknowledge the following in your response:

Analysis of exhibit samples is pending. Be aware that samples of your reformulated batches will be picked up by the field investigational staff.

Please provide any additional stability data which are available to date.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw this application. Your amendment should respond to all the deficiencies listed. A partial reply will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this letter will be considered a MAJOR amendment and should be so designated in your cover letter.

If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

Sincerely yours,

/S/

C. Greg Guyer, Ph.D
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

cc:

Endorsements:

NOT APPROVABLE: MAJOR

1964 THIRTY YEARS 1994

biocraft LABORATORIES, INC.

Noted. To Labeling (Angela) Chem review in turn Mike Anderson 6/17/94

FEDERAL EXPRESS

May 12, 1994

BIOAVAILABILITY
NDA ORIG AMENDMENT
N|AC FPE

Office of Generic Drugs, CDER, FDA
Document Control Room
Metro Park North II
7500 Standish Place, Room #150
Rockville, MD 20855-2773

CORPORATE HEADQUARTERS
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Fax: 201-797-0015

AADA 64-081
CEFACLOR CAPSULES, USP, 250 mg and 500 mg

RE: MAJOR AMENDMENT IN RESPONSE TO FDA DEFICIENCY LETTERS, namely:
- **a) CHEMISTRY: GUYER TO SNYDER, DATED AUGUST 16, 1993**
- **b) BIOEQUIVALENCE: WILLIAMS TO SNYDER, DATED SEPTEMBER 13, 1993**
- **c) LABELING: POLLOCK TO SNYDER, DATED OCTOBER 6, 1993**

Dear Staff:

Reference is made to three FDA Deficiency letters, namely, Guyer to Snyder, dated August 16, 1993; Williams to Snyder, dated September 13, 1993; and Pollock to Snyder, dated October 6, 1993 regarding our AADA 64-081 on Cefaclor Capsules, USP, 250 mg and 500 mg.

This Amendment includes Responses to these three Deficiency Letters. In addition, we have reformulated the Cefaclor Capsules, USP, 250 mg and 500 mg as requested in the letter of Williams to Snyder, dated September 13, 1993. Therefore, in the appropriate sections of this major amendment, new chemistry, manufacturing, and control data have been submitted. We also have included bioequivalence studies using the reformulated product.

As requested in your letters, please find included in this Submission the following:

For A: Chemistry Amendment in response to Deficiency Letter dated August 16, 1993:

1.
2.
3.
4.
5.
6.
7.
8.
9.
10.

002

GENERIC DRUGS

92 Route 46, P.O. Box 185, Elmwood Park, NJ 07407, Phone: 201-796-3436, Fax: 201-796-1434
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5000 Christopher Drive, Mexico, MO 65265, Phone: 314-581-8080, Fax: 314-581-8085

AADA 64-081

AUG 16 1993

Biocraft Laboratories, Inc.
Attention: Jay Snyder
8-10 River Road
Fair Lawn, NJ 07410

Dear Sir:

This is in reference to your abbreviated antibiotic application dated February 22, 1993, submitted pursuant to Section 507 of the Food, Drug, and Cosmetic Act, for Cefaclor Capsules USP, 250 mg and 500 mg.

The application is deficient and, therefore, not approvable under Section 507 of the Act for the following reasons:

A. Chemistry Deficiencies

In addition to responding to these deficiencies, please note and acknowledge the following in your response.

1. Review of the bioequivalence portion of the application and analysis of your samples by our Antimicrobial Drug Branch are pending.

2. Review of your proposed labeling is pending and comments will be sent under separate cover.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw this application. Your amendment should respond to all the deficiencies listed. Partial reply will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this letter will be considered a MAJOR amendment and should be so designated in your cover letter. You will be notified in a separate letter of any deficiencies in the bioequivalence portion of your application. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

Sincerely yours,

/S/ 8/13/93

C. Greg Guyer, Ph.D.
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

cc:

Endorsements: 8/12/93

8/13/93

SEP 13 1993

AADA 64-081

Biocraft Laboratories, Inc.
Attention: Mr. Jay Snyder
18-01 River Road
Fair Lawn, NJ 07410

Dear Sir:

This is in reference to your abbreviated antibiotic application dated February 19, 1993 submitted pursuant to Section 507 of the Federal Food, Drug, and Cosmetic Act, for Cefaclor Capsules USP, 250 mg and 500 mg.

Reference is also made to our letter dated August 16, 1993 informing you of chemistry, manufacturing, controls, and labeling deficiencies. The Division of Bioequivalence has reviewed your bioequivalence data and has determined that the bioequivalence study is deficient under 21 CFR 314.127(a)(6)(i) of the regulations, and that your abbreviated new drug application is not approvable under section 507 of the Act, for the following reason:

> There is a statistically significant difference observed for C_{MAX} between the test product and the reference product under fasting conditions. The least square means for C_{MAX} value was 14.2% lower for the test product than for the reference product. Therefore, the Biocraft study results suggest that the test product (Biocraft) has a slower rate of absorption when compared to that of the reference product under fasting conditions and the 90% confidence interval for C_{MAX} was not within the acceptable range of 80-125%.

The request for a waiver of the bioequivalence study requirements for your Cefaclor Capsules USP 250 mg cannot be considered at this time, since the bioequivalence study for the Cefaclor Capsules USP 500 mg under fasting conditions is regarded as unacceptable. The OGD may consider granting a waiver for the 250 mg capsule, once the 500 mg capsule has passed the requirements of a fasting bioequivalence study. The request for waiver of in vivo bioequivalence requirements for the 250 mg strength of the test product should be resubmitted with the final study report.

For the reasons stated, we regard your bioequivalence study as inadequate to support the approval of this abbreviated new drug application. Therefore, the Office of Generic Drugs will suspend any further review of this application until an amendment containing complete information and data necessary to support approval of the application is submitted.

The file is now closed. You are required to take an action described under 21 CFR 314.120 and 21 CFR 314.96 which will either amend or withdraw the application. **Your amendment should respond to all cited chemistry, labeling and bioequivalence deficiencies stated above and/or in previous letters.** In the event that reformulation of your product is needed to meet the agency's bioequivalence requirements, revised chemistry, manufacturing, controls and labeling data should also be included in the amendment. A partial reply will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. **Your response to this letter will be considered as a major amendment and should be so designated as a "Bioequivalence Major Amendment" in your cover letter.**

Representatives of the Division of Bioequivalence are available to clarify this letter and to assist you in the possible redesign of your study. Please contact Jason A. Gross, Pharm. D. Chief, Consumer Safety Officer at (301) 594-0375 for further assistance.

Sincerely yours,

9/5/93

Roger L. Williams, M.D.
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

CC:

AADA 64-081

Biocraft Laboratories, Inc.
Attention: Jay Snyder
18-01 River Road
P.O. Box 948
Fair Lawn, NJ 07410

Dear Sir:

We acknowledge the receipt of your abbreviated antibiotic application (AADA) submitted pursuant to Section 507 of the Federal Food, Drug and Cosmetic Act for the following:

NAME OF DRUG: Cefaclor Capsules USP, 250 mg and 500 mg

DATE OF APPLICATION: February 19, 1993

DATE OF RECEIPT: March 3, 1993

DATE ACCEPTABLE FOR FILING: April 21, 1993

We will correspond with you further after we have completed the review of your application.

Please be advised that during the AADA approval process, samples of the active and inactive ingredients, and the AADA exhibit batch(es) (which should be the same as the biobatch if a bioequivalence study was conducted) may be collected by the FDA district office staff and tested by FDA district or headquarters laboratory staff. Drug substance standards and manufacturer's documentation of the impurity profile should be made available. In addition, batch records, certificates of analysis and specifications and tests for the drug substance, drug product and inactive ingredients may be collected.

Please refer to the Office of Generic Drugs, Policy and Procedure Guide # 35-92, for the number of batches and the batch size requirements for AADA's submitted for the drug substance and drug product.

The subject product of an AADA must conform to the current official compendial monograph requirements and be compatible with the test and assay methods described in that monograph. You must submit adequate documentation and laboratory data in your AADA that prove that any non-official alternate procedures that you choose to use for the analytical control (release) of your product are equivalent to the official compendial procedures. If this information is not submitted, the review of the application will be delayed.

Please identify any communications concerning this application with the number shown above.

Sincerely yours,

/S/ 1/93

Roger L. Williams, M.D.
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

cc:

HFR-MA300/Mid-Atlantic [illegible]

HFD-84

biocraft
LABORATORIES, INC.

4/23/93 c/Arisd ok to file CS Johnson 4/28/93

Corporate Headquarters
18-01 River Road
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Fax: 201-575-6089

12 Industrial Park
Waldwick, NJ 07463
Phone: 201-445-3141
Fax: 201-445-8564

5000 Christopher Drive
Mexico, MO 65265
Phone: 314-581-8080
Fax: 314-581-8085

FEDERAL EXPRESS

April 13, 1993

N-000/AC

NDA ORIG AMENDMENT

RECEIVED
APR 21 1993
GENERIC DRUGS

Office of Generic Drugs
Food and Drug Administration
Center For Drug Evaluation and Research
Metro Park North #2
Document Control Room #150
HFD-600
7500 Standish Place
Rockville, Maryland 20855

RE: AMENDMENT TO AADA 64-081
CEFACLOR CAPSULES, USP, 250 mg and 500 mg

Dear Staff:

Reference is made to FDA Letter, Williams to Snyder, dated April 5, 1993, (see attached) regarding our AADA Submission on Cefaclor Capsules, USP, 250 mg and 500 mg.

As requested in your letter, attached please find DMF letter of authorization from the holder of the application on the bulk drug Cefaclor.

Additionally, as further requested in your letter, please find included in this Submission the master production batch records for the largest batch intended for production, the batch size which is a ten-fold scale-up or less, from the batch used to conduct the bioequivalence test.

...1 accordingly. Thank you.

final print under labels 1980 1983 375 mg/5 mL 50 mL CL

Sincerely,

BIOCRAFT LABORATORIES, INC.

Nora Buenviaje
Regulatory Associate

NB/kn
Enclosures

ORIGINAL

AADA 64-081

Biocraft Laboratories, Inc.
Attention: Jay Snyder
18-01 River Road
Fair Lawn, NJ 07410

OCT 6 1993

Dear Sir:

Please refer to your abbreviated antibiotic application dated February 19, 1993, submitted pursuant to Section 507 of the Federal Food, Drug, and Cosmetic Act for Cefaclor Capsules USP, 250 mg and 500 mg.

Reference is also made to our letter of August 16, 1993, noting that this application is not approvable and outlining the deficiencies. This letter will provide for the review of labels and labeling only, as noted in the above cited communication.

CONTAINER {15's, 100's, and 500's - 250 mg and 500 mg}

1. Usual Adult Dosage ["Dosage" rather than "Dose"]

2. ...15°-30°C (59°-86°F).

INSERT

General Comments

We refer you to the amendments of August 5, 1993, to your related applications for Cefaclor for Oral Suspension USP (AADA's 64-074, 64-077, 64-078, 64-079), in which you submitted insert labeling. Please use that insert labeling as the model for your cefaclor capsule labeling, as appropriate for the capsule dosage form.

In addition, in the INDICATIONS AND USAGE and the DOSAGE AND ADMINISTRATION sections, revise the first line from "Cefaclor is..." to "Cefaclor capsules are...".

Please revise your container labels and package insert labeling, then submit final print (or draft, if you prefer).

Should further information become available relating to the safety and efficacy of this product, you may be asked to further revise your labeling prior to approval.

The file is now closed. Please refer again to our letter of August 16, 1993, explaining the requirements for reopening the file for this application.

Sincerely yours,

/S/ 10/6/93

Robert W. Pollock
Director, Division of Labeling and
Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: AADA#: 64-081

1583

AADA 64-081

Biocraft Laboratories, Inc.
Attention: Jay Snyder
18-01 River Road
P.O. Box 948
Fair Lawn, NJ 07410

Dear Sir:

Please refer to your abbreviated antibiotic application (AADA) submitted under Section 507 of the Federal Food, Drug and Cosmetic Act for Cefaclor Capsules USP, 250 mg and 500 mg.

We have given your AADA a preliminary review, and we find that it is not sufficiently complete to merit substantive review. Thus, it will not be filed as an abbreviated antibiotic application within the meaning of Section 507 of the Act.

We are refusing to file this AADA under CFR 314.101(d)(3) for the following reason:

> Please be advised that authorization is required from the holder of the application for the bulk drug in order for the agency to reference the application. We note that you have provided authorization from the U.S. agent. Please provide authorization from the holder of the application for the bulk drug that allows the U.S. agent to grant authorization to review the application. Alternatively, the applicant for the bulk drug may provide a letter of authorization specifically referencing your proposed products and corporate name.
>
> We note that you have included blank master production batch records. Please refer to the letter from the Director, Office of Generic Drugs, dated November 8, 1991, referring to completeness of submissions. The letter states that the master production batch record should be submitted for the largest batch intended for production (note that under Policy and Procedure Guide 22-90, revised September 13, 1990, approval cannot be given for more that a ten-fold scale-up from the batch used to conduct the bioequivalence test).

Within 30 days of the date of this letter, you may amend your application to include the above information or request in

writing an informal conference about our refused to file the application. To file this application over FDA's protest, you must avail yourself of this informal conference.

If after the informal conference, you still do not agree with our conclusions, you may make a written request to file the application over protest, as authorized by 21 CFR 314.101(c). If you do so the application shall be filed over protest under 21 CFR 314.101(b). The filing date will be 60 days after the date you requested the informal conference. If you have any questions please call:

Ceceila N. Parise, R.Ph.
Consumer Safety Officer
(301) 295-8315

Sincerely yours,

/S/

4-5-93

Roger L. Williams, M.D.
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

cc:

4-2-93
4/2/93